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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:43:04 ON 23 DEC 2004

=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 16:43:10 ON 23 DEC 2004

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FILE 'BIOSIS' ENTERED AT 16:43:10 ON 23 DEC 2004
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FILE 'SCISEARCH' ENTERED AT 16:43:10 ON 23 DEC 2004
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=> s traf2 or (traf 2) or (traf-2)
L1        2357 TRAF2 OR (TRAF 2) OR (TRAF-2)

=> s antisense or anti (2n) sense or (compleme? (2n) (oligonucl? or nucle?))
   3 FILES SEARCHED...
L2      146629 ANTISENSE OR ANTI (2N) SENSE OR (COMPLEME? (2N) (OLIGONUCL? OR
               NUCLE?))

=> s l2 and l1
L3          67 L2 AND L1

=> s l2 (P) l1
L4          47 L2 (P) L1

=> s l1 (s) l2
L5          22 L1 (S) L2

=> dup rem l4
PROCESSING COMPLETED FOR L4
L6           15 DUP REM L4 (32 DUPLICATES REMOVED)

=> s BAKER, B?/au;s COWSERT, L?/au;s MONIA, B?/au;s XU, X?/au
L7        6396 BAKER, B?/AU


S COWSERT, IS NOT A RECOGNIZED COMMAND
COMMAND STACK INTERRUPTED.  ENTER "DISPLAY HISTORY"
TO SEE WHICH COMMANDS WERE EXECUTED.

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s COWSERT, L?/au;s MONIA, B?/au;s XU, X?/au
S COWSERT, IS NOT A RECOGNIZED COMMAND
COMMAND STACK INTERRUPTED.  ENTER "DISPLAY HISTORY"
TO SEE WHICH COMMANDS WERE EXECUTED.

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s cowsert, L?/au; s MONIA, B?/au;s XU, X?/au
L8         438 COWSERT, L?/AU


S MONIA, IS NOT A RECOGNIZED COMMAND
COMMAND STACK INTERRUPTED.  ENTER "DISPLAY HISTORY"
TO SEE WHICH COMMANDS WERE EXECUTED.
```

```
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s MONIA, B?/au;s XU, X?/au
L9          912 MONIA, B?/AU


L10       25068 XU, X?/AU

=> s l7 or l8 or l9 or l10
L11       32652 L7 OR L8 OR L9 OR L10

=> d his

     (FILE 'HOME' ENTERED AT 16:43:04 ON 23 DEC 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 16:43:10 ON 23
     DEC 2004
L1          2357 S TRAF2 OR (TRAF 2) OR (TRAF-2)
L2        146629 S ANTISENSE OR ANTI (2N) SENSE OR (COMPLEME? (2N) (OLIGONUCL? O
L3             67 S L2 AND L1
L4             47 S L2 (P) L1
L5             22 S L1 (S) L2
L6             15 DUP REM L4 (32 DUPLICATES REMOVED)
L7           6396 S BAKER, B?/AU
L8            438 S COWSERT, L?/AU
L9            912 S MONIA, B?/AU
L10         25068 S XU, X?/AU
L11         32652 S L7 OR L8 OR L9 OR L10

=> s l11 and l1
L12           10 L11 AND L1

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13            3 DUP REM L12 (7 DUPLICATES REMOVED)

=> s l13 or l6
L14           17 L13 OR L6

=> s l14 and py=<1998
   2 FILES SEARCHED...
L15            0 L14 AND PY=<1998

=> s l14 and py=<2002
   2 FILES SEARCHED...
   4 FILES SEARCHED...
L16           15 L14 AND PY=<2002

=> dup rem l3
PROCESSING COMPLETED FOR L3
L17           31 DUP REM L3 (36 DUPLICATES REMOVED)

=> s l13 or l17
L18           33 L13 OR L17

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19           33 DUP REM L18 (0 DUPLICATES REMOVED)

=> s l19 and py=<1999
   2 FILES SEARCHED...
   4 FILES SEARCHED...
```

```
L20          8 L19 AND PY=<1999

=> s tumor (3n) necrosis (3n) factor (3n) type (3n) 2 (3n) receptor (3N) associated
(3n) protein
   3 FILES SEARCHED...
L21          8 TUMOR (3N) NECROSIS (3N) FACTOR (3N) TYPE (3N) 2 (3N) RECEPTOR
                (3N) ASSOCIATED (3N) PROTEIN

=> s trap3
L22          8 TRAP3

=> s l21 or l22
L23         14 L21 OR L22

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24          11 DUP REM L23 (3 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 16:43:04 ON 23 DEC 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 16:43:10 ON 23
     DEC 2004
L1         2357 S TRAF2 OR (TRAF 2) OR (TRAF-2)
L2       146629 S ANTISENSE OR ANTI (2N) SENSE OR (COMPLEME? (2N) (OLIGONUCL? O
L3           67 S L2 AND L1
L4           47 S L2 (P) L1
L5           22 S L1 (S) L2
L6           15 DUP REM L4 (32 DUPLICATES REMOVED)
L7         6396 S BAKER, B?/AU
L8          438 S COWSERT, L?/AU
L9          912 S MONIA, B?/AU
L10       25068 S XU, X?/AU
L11       32652 S L7 OR L8 OR L9 OR L10
L12          10 S L11 AND L1
L13           3 DUP REM L12 (7 DUPLICATES REMOVED)
L14          17 S L13 OR L6
L15           0 S L14 AND PY=<1998
L16          15 S L14 AND PY=<2002
L17          31 DUP REM L3 (36 DUPLICATES REMOVED)
L18          33 S L13 OR L17
L19          33 DUP REM L18 (0 DUPLICATES REMOVED)
L20           8 S L19 AND PY=<1999
L21           8 S TUMOR (3N) NECROSIS (3N) FACTOR (3N) TYPE (3N) 2 (3N) RECEPTO
L22           8 S TRAP3
L23          14 S L21 OR L22
L24          11 DUP REM L23 (3 DUPLICATES REMOVED)

=> s l23 or l1
L25        2368 L23 OR L1

=> s l25 (P) l2
L26          47 L25 (P) L2

=> s l26 not l4
L27           0 L26 NOT L4

=> s l4 (s) (inhib? or reduc?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L19 (S) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L20 (S) '
   3 FILES SEARCHED...
```

```
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L22 (S) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L23 (S) '
L28          36 L4 (S) (INHIB? OR REDUC?)

=> s l1 (s) (inhib? or reduc?)
   1 FILES SEARCHED...
L29         887 L1 (S) (INHIB? OR REDUC?)

=> s (l1 or l24) (s) (inhib? or reduc?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L179) (S) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L183) (S) '
L30         920 (L1 OR L24) (S) (INHIB? OR REDUC?)

=> d his

     (FILE 'HOME' ENTERED AT 16:43:04 ON 23 DEC 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 16:43:10 ON 23
     DEC 2004
L1          2357 S TRAF2 OR (TRAF 2) OR (TRAF-2)
L2        146629 S ANTISENSE OR ANTI (2N) SENSE OR (COMPLEME? (2N) (OLIGONUCL? O
L3            67 S L2 AND L1
L4            47 S L2 (P) L1
L5            22 S L1 (S) L2
L6            15 DUP REM L4 (32 DUPLICATES REMOVED)
L7          6396 S BAKER, B?/AU
L8           438 S COWSERT, L?/AU
L9           912 S MONIA, B?/AU
L10        25068 S XU, X?/AU
L11        32652 S L7 OR L8 OR L9 OR L10
L12           10 S L11 AND L1
L13            3 DUP REM L12 (7 DUPLICATES REMOVED)
L14           17 S L13 OR L6
L15            0 S L14 AND PY=<1998
L16           15 S L14 AND PY=<2002
L17           31 DUP REM L3 (36 DUPLICATES REMOVED)
L18           33 S L13 OR L17
L19           33 DUP REM L18 (0 DUPLICATES REMOVED)
L20            8 S L19 AND PY=<1999
L21            8 S TUMOR (3N) NECROSIS (3N) FACTOR (3N) TYPE (3N) 2 (3N) RECEPTO
L22            8 S TRAP3
L23           14 S L21 OR L22
L24           11 DUP REM L23 (3 DUPLICATES REMOVED)
L25         2368 S L23 OR L1
L26           47 S L25 (P) L2
L27            0 S L26 NOT L4
L28           36 S L4 (S) (INHIB? OR REDUC?)
L29          887 S L1 (S) (INHIB? OR REDUC?)
L30          920 S (L1 OR L24) (S) (INHIB? OR REDUC?)

=> s l1 or l23
L31         2368 L1 OR L23

=> s l31 (s) (INHIB? OR REDUC?)
L32          888 L31 (S) (INHIB? OR REDUC?)

=> s l31 (5n) (INHIB? OR REDUC?)
L33          413 L31 (5N) (INHIB? OR REDUC?)

=> s l31 (3n) (INHIB? OR REDUC?)
```

L34 326 L31 (3N) (INHIB? OR REDUC?)

=> dup rem l34
PROCESSING COMPLETED FOR L34
L35 84 DUP REM L34 (242 DUPLICATES REMOVED)

=> s l35 py<=1998
MISSING OPERATOR L35 PY<=1998
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l35 and py<=1998
2 FILES SEARCHED...
4 FILES SEARCHED...
L36 23 L35 AND PY<=1998

=> d l36 1-23 ibib abs

L36 ANSWER 1 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1999030399 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9813034
TITLE: Nuclear factor kB-independent cytoprotective pathways originating at tumor necrosis factor receptor-associated factor 2.
AUTHOR: Natoli G; Costanzo A; Guido F; Moretti F; Bernardo A; Burgio V L; Agresti C; Levrero M
CORPORATE SOURCE: Fondazione Andrea Cesalpino, Policlinico Umberto I, University of Rome La Sapienza, Viale del Policlinico 155, 00161 Rome, Italy.
SOURCE: Journal of biological chemistry, **(1998 Nov 20)** 273 (47) 31262-72.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20020919
Entered Medline: 19981221

AB Most normal and neoplastic cell types are resistant to tumor necrosis factor (TNF) cytotoxicity unless cotreated with protein or RNA synthesis inhibitors, such as cycloheximide and actinomycin D. Cellular resistance to TNF requires TNF receptor-associated factor 2 (TRAF2), which has been hypothesized to act mainly by mediating activation of the transcription factors nuclear factor kB (NFkB) and activator protein 1 (AP1). NFkB was proposed to switch on transcription of yet unidentified anti-apoptotic genes. To test the possible existence of NFkB-independent cytoprotective pathways, we systematically compared selective trans-dominant inhibitors of the NFkB pathway with **inhibitors** of **TRAF2** signaling for their effect on TNF cytotoxicity. Blockade of TRAF2 function(s) by signaling-deficient oligomerization partners or by molecules affecting TRAF2 recruitment to the TNF receptor 1 complex completely abrogated the cytoprotective response. Conversely, sensitization to TNF cytotoxicity induced by a selective NFkB blockade affected only a fraction of TNF-treated cells in an apparently stochastic manner. No cytoprotective role for c-Jun amino-terminal kinases/stress-activated protein kinases (JNKs/SAPKs), which are activated by TRAF2 and contribute to stimulation of activator protein 1 activity, could be demonstrated in the cellular systems tested. Although required for cytoprotection, TRAF2 is not sufficient to protect cells from TNF + cycloheximide cytotoxicity when overexpressed in transfected cells, thus indicating an essential role of additional TNF receptor 1 complex components in the cytoprotective response. Our results indicate that TNF-induced cytoprotection is a

complex function requiring the integration of multiple signal transduction pathways.

L36 ANSWER 2 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1999008537 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9794406
TITLE: NF-kappaB activation in CD27 signaling: involvement of TNF receptor-associated factors in its signaling and identification of functional region of CD27.
AUTHOR: Yamamoto H; Kishimoto T; Minamoto S
CORPORATE SOURCE: Department of Medicine III, Osaka University Medical School, Japan.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), **(1998 Nov 1)** 161 (9) 4753-9.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981118

AB CD27 belongs to TNF receptor family, and it is unique in this family for its disulfide-linked homodimerization of 55-kDa monomers. In the present study we demonstrate that overexpression of CD27 in 293 cells induces a low level of NF-kappaB activation, and the ligation of the receptor by its corresponding ligand (CD70) augments this signal dramatically. Either TNF receptor-associated factor-2 (TRAF2) or TRAF3 binds to the CD27 molecule from the coimmunoprecipitation experiment. This NF-kappaB activation signal is **inhibited** by dominant negative **TRAF2** or intact TRAF3, indicating that TRAF2 and TRAF3 works as a mediator and an inhibitor, respectively. The activated NF-kappaB complex contains at least two components, p50 and p65, but not p52. All these phenomena have also been observed in the TNF receptor type II, CD30 and CD40 signaling system, indicating that this receptor family uses the common or similar molecules for this signal. Finally, we identified the 13-amino acid alignment in the cytoplasmic region of the CD27 molecule (residues 238-250 amino acids), which is critical for the NF-kappaB activation signal and also for its association with TRAFs. This amino acid alignment contains the EEEG sequence, which is essential for interaction of CD30 or CD40 with TRAFs (TRAF1 and TRAF2, but not TRAF3), and also contains the PIQED sequence, which is similar to PXQXT that is known to be necessary for interaction of TNF receptor II and CD30 with TRAFs (TRAF1, 2, and 3).

L36 ANSWER 3 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998448103 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9774977
TITLE: ASK1 is essential for JNK/SAPK activation by TRAF2.
AUTHOR: Nishitoh H; Saitoh M; Mochida Y; Takeda K; Nakano H; Rothe M; Miyazono K; Ichijo H
CORPORATE SOURCE: Department of Biochemistry, Cancer Institute, Tokyo, Japan.
SOURCE: Molecular cell, **(1998 Sep)** 2 (3) 389-95.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981102

AB Tumor necrosis factor (TNF)-induced activation of the c-jun N-terminal kinase (JNK, also known as SAPK; stress-activated protein kinase) requires

TNF receptor-associated factor 2 (TRAF2). The apoptosis signal-regulating kinase 1 (ASK1) is activated by TNF and stimulates JNK activation. Here we show that ASK1 interacts with members of the TRAF family and is activated by TRAF2, TRAF5, and TRAF6 overexpression. A truncated derivative of **TRAF2**, which **inhibits** JNK activation by TNF, blocks TNF-induced ASK1 activation. A catalytically inactive mutant of ASK1 is a dominant-negative **inhibitor** of TNF- and **TRAF2**-induced JNK activation. In untransfected mammalian cells, ASK1 rapidly associates with TRAF2 in a TNF-dependent manner. Thus, ASK1 is a mediator of TRAF2-induced JNK activation.

L36 ANSWER 4 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998447691 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9774460
TITLE: The TRAF family of signal transducers mediates NF-kappaB activation by the TRANCE receptor.
AUTHOR: Wong.B R; Josien R; Lee S Y; Vologodskaia M; Steinman R M; Choi Y
CORPORATE SOURCE: Laboratory of Immunology, The Rockefeller University, New York, New York 10021, USA.
CONTRACT NUMBER: AI13013 (NIAID)
AI41082 (NIAID)
GM07739 (NIGMS)
SOURCE: Journal of biological chemistry, **(1998 Oct 23)** 273 (43) 28355-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF013170
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981112

AB Tumor necrosis factor (TNF)-related activation-induced cytokine (TRANCE), a member of the TNF family expressed on activated T-cells, bone marrow stromal cells, and osteoblasts, regulates the function of dendritic cells (DC) and osteoclasts. The TRANCE receptor (TRANCE-R), recently identified as receptor activator of NF-kappabeta (RANK), activates NF-kappaB, a transcription factor critical in the differentiation and activation of those cells. In this report we identify the TNF receptor-associated factor (TRAF) family of signal transducers as important components of TRANCE-R-mediated NF-kappaB activation. Coimmunoprecipitation experiments suggested potential interactions between the cytoplasmic tail of TRANCE-R with TRAF1, TRAF2, TRAF3, TRAF5, and TRAF6. Dominant negative forms of TRAF2, TRAF5, and TRAF6 and an endogenous **inhibitor** of **TRAF2**, TRAF-interacting protein (TRIP), substantially inhibited TRANCE-R-mediated NF-kappaB activation, suggesting a role of TRAFs in regulating DC and osteoclast function. Overexpression of combinations of TRAF dominant negative proteins revealed competition between TRAF proteins for the TRANCE-R and the possibility of a TRAF-independent NF-kappaB pathway. Analysis of TRANCE-R deletion mutants suggested that the TRAF2 and TRAF5 interaction sites were restricted to the C-terminal 93 amino acids (C-region). TRAF6 also complexed to the C-region in addition to several regions N-terminal to the TRAF2 and TRAF5 association sites. Furthermore, transfection experiments with TRANCE-R deletion mutants revealed that multiple regions of the TRANCE-R can mediate NF-kappaB activation.

L36 ANSWER 5 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998438588 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9763618
TITLE: Stimulus-dependent synergism of the antiapoptotic tumor

necrosis factor receptor-associated factor 2 (TRAF2) and nuclear factor kappaB pathways.

AUTHOR: Lee S Y; Kaufman D R; Mora A L; Santana A; Boothby M; Choi Y

CORPORATE SOURCE: Department of Pathology, Hallym Medical School, Choonchun, Kangwon-do, 200-702, Korea.

CONTRACT NUMBER: AI-36997 (NIAID)

SOURCE: Journal of experimental medicine, **(1998 Oct 5)** 188 (7) 1381-4.
Journal code: 2985109R. ISSN: 0022-1007.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199811

ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20020919
Entered Medline: 19981116

AB Tumor necrosis factor (TNF) signaling leads to pleiotropic responses in a wide range of cell types, in part by activating antiapoptotic and proapoptotic signaling pathways. Thus, although TNF can cause apoptosis and may prove useful in the treatment of malignancies, most cells are resistant to TNF-induced cell death unless de novo protein synthesis is inhibited. Previous studies suggested that TNF activation of the nuclear factor (NF)-kappaB transcription factor family antagonizes the proapoptotic signals initiated by TNF-alpha. TNF receptor-associated factor (TRAF)2 has also been shown to mediate crucial antiapoptotic signals during TNF stimulation, yet is not essential in activation of NF-kappaB under physiologic conditions, thus raising questions about the relationship between these antiapoptotic pathways. We report here that **inhibition** of **TRAF2** and NF-kappaB function in primary cells, by coexpression of a constitutive repressor of multiple NF-kappaB/Rel proteins (IkappaBalpha.DN) and a dominant negative form of TRAF2 (TRAF2.DN), synergistically enhanced TNF-induced apoptosis. The effects were stimulus dependent, such that neither inhibitory molecule affected Fas- and daunorubicin-induced apoptosis to the same degree as TNF-induced death. These findings indicate that the NF-kappaB and TRAF2 pathways activate independent antiapoptotic mechanisms which act in concert to suppress the proapoptotic signals induced by TNF-alpha.

L36 ANSWER 6 OF 23 MEDLINE on STN

ACCESSION NUMBER: 1998404275 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9733516

TITLE: NF-kappaB antiapoptosis: induction of TRAF1 and TRAF2 and c-IAP1 and c-IAP2 to suppress caspase-8 activation.

AUTHOR: Wang C Y; Mayo M W; Korneluk R G; Goeddel D V; Baldwin A S Jr

CORPORATE SOURCE: Department of Endodontics, School of Dentistry, Lineberger Comprehensive Cancer Center, and Curriculum in Genetics and Molecular Biology, University of North Carolina, Chapel Hill, NC 27599-7295, USA.

CONTRACT NUMBER: AI35098 (NIAID)
CA 75080 (NCI)
CA73756 (NCI)
+

SOURCE: Science, **(1998 Sep 11)** 281 (5383) 1680-3.
Journal code: 0404511. ISSN: 0036-8075.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199810

ENTRY DATE: Entered STN: 19981020
Last Updated on STN: 20000303

Entered Medline: 19981007

AB Tumor necrosis factor alpha (TNF-alpha) binding to the TNF receptor (TNFR) potentially initiates apoptosis and activates the transcription factor nuclear factor kappa B (NF-kappaB), which suppresses apoptosis by an unknown mechanism. The activation of NF-kappaB was found to block the activation of caspase-8. TRAF1 (TNFR-associated factor 1), **TRAF2**, and the **inhibitor**-of-apoptosis (IAP) proteins c-IAP1 and c-IAP2 were identified as gene targets of NF-kappaB transcriptional activity. In cells in which NF-kappaB was inactive, all of these proteins were required to fully suppress TNF-induced apoptosis, whereas c-IAP1 and c-IAP2 were sufficient to suppress etoposide-induced apoptosis. Thus, NF-kappaB activates a group of gene products that function cooperatively at the earliest checkpoint to suppress TNF-alpha-mediated apoptosis and that function more distally to suppress genotoxic agent-mediated apoptosis.

L36 ANSWER 7 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998381580 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9705938
TITLE: Identification of CARDIAK, a RIP-like kinase that associates with caspase-1.
AUTHOR: Thome M; Hofmann K; Burns K; Martinon F; Bodmer J L; Mattmann C; Tschopp J
CORPORATE SOURCE: Institute of Biochemistry, University of Lausanne, Epalinges, Switzerland.
SOURCE: Current biology : CB, **(1998 Jul 16)** 8 (15) 885-8. Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF064824
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981120

AB Members of the tumor necrosis factor receptor (TNFR) superfamily have an important role in the induction of cellular signals resulting in cell growth, differentiation and death. TNFR-1 recruits and assembles a signaling complex containing a number of death domain (DD)-containing proteins, including the adaptor protein TRADD and the serine/threonine kinase RIP, which mediates TNF-induced NF-kappa B activation. RIP also recruits caspase-2 to the TNFR-1 signaling complex via the adaptor protein RAIDD, which contains a DD and a caspase-recruiting domain (CARD). Here, we have identified a RIP-like kinase, termed CARDIAK (for CARD-containing interleukin (IL)-1 beta converting enzyme (ICE) associated kinase), which contains a serine/threonine kinase domain and a carboxy-terminal CARD. Overexpression of CARDIAK induced the activation of both NF-kappa B and Jun N-terminal kinase (JNK). CARDIAK interacted with the TNFR-associated factors TRAF-1 and TRAF-2, and a dominant-negative form of **TRAF-2 inhibited** CARDIAK-induced NF-kappa B activation. Interestingly, CARDIAK specifically interacted with the CARD of caspase-1 (previously known as ICE), and this interaction correlated with the processing of pro-caspase-1 and the formation of the active p20 subunit of caspase-1. Together, these data suggest that CARDIAK may be involved in NF-kappa B/JNK signaling and in the generation of the proinflammatory cytokine IL-1 beta through activation of caspase-1.

L36 ANSWER 8 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998157982 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9488716
TITLE: Activation of OX40 signal transduction pathways leads to tumor necrosis factor receptor-associated factor (TRAF) 2- and TRAF5-mediated NF-kappaB activation.

AUTHOR: Kawamata S; Hori T; Imura A; Takaori-Kondo A; Uchiyama T
CORPORATE SOURCE: Institute for Virus Research, Kyoto University, Kyoto 606, Japan.
SOURCE: Journal of biological chemistry, **(1998 Mar 6)** 273 (10) 5808-14.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980416
Last Updated on STN: 19980416
Entered Medline: 19980407

AB We investigated the intracellular signaling of OX40, a member of the tumor necrosis factor receptor family. Activation of NF-kappaB in OX40-transfected HSB-2 cells was detected by electrophoretic mobility shift assay within 30 min after the binding of the ligand gp34. In vitro binding experiments showed that tumor necrosis factor receptor-associated factor (TRAF) 1, TRAF2, TRAF3, and TRAF5 but not TRAF4 associated with glutathione S-transferase-OX40 fusion protein. The cotransfection experiments using human embryo kidney cell derived HEK 293T cells showed that TRAF2, TRAF3, and TRAF5 associated with OX40 in vivo. Studies with OX40 deletion mutants demonstrated that the cytoplasmic portion consisting of amino acid sequence 256-263 (GGSFRTPI) was required for the association with TRAFs and NF-kappaB activation. The introduction of the dominant negative mutants of TRAF2 and TRAF5 into HSB-2-OX40 cells suppressed NF-kappaB activation in a dose-dependent manner. In addition, the introduction of TRAF3 together with the dominant negative mutants of **TRAF2** or TRAF5 further **reduced** NF-kappaB activation.
These results indicate that the NF-kappaB activation resulting from OX40 stimulation is mediated by both TRAF2 and TRAF5, and is likely to be negatively modulated by TRAF3.

L36 ANSWER 9 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998129826 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9461607
TITLE: Tumor necrosis factor receptor (TNFR)-associated factor 2A (TRAF2A), a TRAF2 splice variant with an extended RING finger domain that inhibits TNFR2-mediated NF-kappaB activation.
AUTHOR: Brink R; Lodish H F
CORPORATE SOURCE: Whitehead Institute for Biomedical Research, Cambridge, Massachusetts 02142, USA.. R.Brink@centenary.usyd.edu.au
CONTRACT NUMBER: R01 CA-63260 (NCI)
SOURCE: Journal of biological chemistry, **(1998 Feb 13)** 273 (7) 4129-34.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF027570
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980323

AB We describe here the identification and characterization of tumor necrosis factor receptor (TNFR)-associated factor 2A (TRAF2A), a splice variant of the TRAF2 molecule utilized for signal transduction by members of the TNFR family. TRAF2A and TRAF2 cDNAs are identical in sequence with the exception of an extra 21 base pairs of sequence encoding a 7-amino acid insert within the TRAF2A RING finger domain. TRAF2A mRNA expression is regulated in a tissue-specific manner, with relative TRAF2A mRNA levels

being highest in spleen and lowest in brain. TRAF2A protein is capable of binding to the cytoplasmic domain of TNFR2 (p75) and is detectable in T-lymphoma cells stably transfected with the TRAF2A cDNA. Unlike TRAF2, TRAF2A has a short half-life (approximately 100 min) in these cells and is expressed at only low levels in transiently transfected COS-7 cells. However, TRAF2A levels in transiently transfected COS-7 cells approach those of TRAF2 upon coexpression with TRAF1 and/or TRAF2, indicating that TRAF2A stability is regulated by the binding of other TRAF family proteins. Also in contrast to TRAF2, TRAF2A is unable to stimulate NF-kappaB activity when overexpressed in 293 cells and acts as a dominant inhibitor of TNFR2-dependent NF-kappaB activation. TRAF2A thus represents a novel signal transduction protein, the expression of which can act to **inhibit TRAF2**-dependent NF-kappaB activation.

L36 ANSWER 10 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998118552 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9435232
TITLE: UVB-induced association of tumor necrosis factor (TNF) receptor 1/TNF receptor-associated factor-2 mediates activation of Rel proteins.
AUTHOR: Tobin D; van Hogerlinden M; Toftgard R
CORPORATE SOURCE: Department of Bioscience at Novum, Karolinska Institute, NOVUM, Huddinge, Sweden.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1998 Jan 20)** 95 (2) 565-9.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980224

AB Exposure of mammalian skin to UV light results in induced gene transcription, playing a role in inflammation, immunosuppression, and tumor promotion. One important group of transcription factors induced by UV radiation is composed of members of the Rel/NF-kappa B family, which are known to play a major role in the transcriptional activation of many genes encoding inflammatory cytokines, adhesion molecules, and viral proteins. However, the upstream events in the transduction of the UVB signal to Rel protein activity are, as yet, unknown. Here, we provide biochemical evidence that exposure of keratinocytes to UVB causes rapid association of tumor necrosis factor (TNF) receptor 1 with its downstream partner TRAF-2. The functional relevance of this association is demonstrated by experiments showing that expression of a dominant negative TNF receptor 1 or **TRAF-2** protein **inhibits** UVB-induced Rel-dependent transcription. Inclusion of a neutralizing antibody toward TNF alpha has no effect on UVB activation of a Rel-responsive reporter gene. Therefore, UVB-induced activation of Rel proteins via TNF receptor 1, independent of ligand activation, is a key component in the UV response in keratinocytes.

L36 ANSWER 11 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998070373 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9405407
TITLE: Activation of stress-activated protein kinase/c-Jun N-terminal kinase, but not NF-kappaB, by the tumor necrosis factor (TNF) receptor 1 through a TNF receptor-associated factor 2- and germinal center kinase related-dependent pathway.
AUTHOR: Shi C S; Kehrl J H
CORPORATE SOURCE: B Cell Molecular Immunology Section, Laboratory of

Immunoregulation, NIAID, National Institutes of Health, Bethesda, Maryland 20892-1876, USA.

SOURCE: Journal of biological chemistry, **(1997 Dec 19)** 272 (51) 32102-7.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980130
Last Updated on STN: 20020420
Entered Medline: 19980122

AB A key step by which tumor necrosis factor (TNF) signals the activation of nuclear factor-kappaB (NF-kappaB) and the stress-activated protein kinase (SAPK, also called c-Jun N-terminal kinase or JNK) is the recruitment to the TNF receptor of TNF receptor-associated factor 2 (TRAF2). However, the subsequent steps in TRAF2-induced SAPK and NF-kappaB activation remain unresolved. Here we report the identification of a TNF-responsive serine/threonine protein kinase termed GCK related (GCKR) that likely signals via mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) kinase kinase 1 (MEKK1) to activate the SAPK pathway. TNF, TRAF2, and ultraviolet (UV) light, which in part uses the TNF receptor signaling pathway, all increased GCKR activity. A **TRAF2** mutant, which **inhibits** both **TRAF2** -induced NF-kappaB and SAPK activation, blocked TNF-induced GCKR activation. Finally, interference with GCKR expression impeded TRAF2- and TNF-induced SAPK activation but not that of NF-kappaB. This suggests a divergence in the TNF signaling pathway that leads to SAPK and NF-kappaB activation, which is located downstream of TRAF2 but upstream of GCKR.

L36 ANSWER 12 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998051059 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9390693
TITLE: TRAF2 is essential for JNK but not NF-kappaB activation and regulates lymphocyte proliferation and survival.
AUTHOR: Lee S Y; Reichlin A; Santana A; Sokol K A; Nussenzweig M C; Choi Y
CORPORATE SOURCE: Laboratory of Immunology, The Rockefeller University, New York, New York 10021, USA.
SOURCE: Immunity, **(1997 Nov)** 7 (5) 703-13.
Journal code: 9432918. ISSN: 1074-7613.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971217

AB TRAF2 is believed to mediate the activation of NF-kappaB and JNK induced by the tumor necrosis factor receptor (TNFR) superfamily, which elicits pleiotropic responses in lymphocytes. We have investigated the physiological roles of TRAF2 in these processes by expressing a lymphocyte-specific dominant negative form of TRAF2, thereby blocking this protein's effector function. We find that the TNFR superfamily signals require TRAF2 for activation of JNK but not NF-kappaB. In addition, we show that TRAF2 induces NF-kappaB-independent antiapoptotic pathways during TNF-induced apoptosis. **Inhibition** of **TRAF2** leads to splenomegaly, lymphadenopathy, and an increased number of B cells. These findings indicate that TRAF2 is involved in the regulation of lymphocyte function and growth in vivo.

L36 ANSWER 13 OF 23 MEDLINE on STN

ACCESSION NUMBER: 1998026141 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9379019
TITLE: CD40-mediated signals inhibit the binding of TNF receptor-associated factor 2 to the CD40 cytoplasmic domain.
AUTHOR: Chaudhuri A; Orme S; Eilam S; Cherayil B J
CORPORATE SOURCE: Mucosal Immunology Laboratory, Combined Program in Pediatric Gastroenterology and Nutrition, Massachusetts General Hospital, Charlestown 02129, USA.
CONTRACT NUMBER: T-32-DK-07477 (NIDDK)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), **(1997 Nov 1)** 159 (9) 4244-51.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971112

AB TNF receptor-associated factor 2 (TRAF2) is a signal-transducing protein associated with the CD40 cytoplasmic domain. It has been hypothesized that during signal transduction, TRAF2 must be released from CD40 in order for it to interact with downstream signaling molecules. We found that CD40 and TRAF2 were constitutively associated with each other in a human B cell line. Following stimulation with an anti-CD40 Ab, a decrease in the amount of CD40-associated TRAF2 was observed that could not be explained by a change in total level of either of the proteins. These results, as well as similar findings obtained with 293 cells overexpressing CD40 and TRAF2, suggested that CD40-mediated signals **inhibited** the CD40-**TRAF2** interaction. We then conducted binding studies using CD40 cytoplasmic domain fusion proteins and TRAF2 derived from either control or CD40-stimulated cell lines. These in vitro studies also indicated that the binding of TRAF2 to the CD40 cytoplasmic domain was inhibited by CD40 stimulation. The results of these experiments, as well as differences between the in vitro and in vivo findings, indicated that multiple mechanisms were involved in the **inhibition** of the CD40-**TRAF2** interaction by CD40 signals. Possible mechanisms of inhibition are discussed based on mapping of the TRAF2 binding site on the CD40 cytoplasmic domain.

L36 ANSWER 14 OF 23 MEDLINE on STN
ACCESSION NUMBER: 97461469 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9317150
TITLE: TNF initiates E-selectin transcription in human endothelial cells through parallel TRAF-NF-kappa B and TRAF-RAC/CDC42-JNK-c-Jun/ATF2 pathways.
AUTHOR: Min W; Pober J S
CORPORATE SOURCE: Molecular Cardiobiology Program, Boyer Center for Molecular Medicine, Yale University School of Medicine, New Haven, CT 06536, USA.
CONTRACT NUMBER: R37-HL36003 (NHLBI)
T32-AI07019-21 (NIAID)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), **(1997 Oct 1)** 159 (7) 3508-18.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 20021015

Entered Medline: 19971021

AB TNF acts on the E-selectin gene promoter at three kappa B elements and at a variant cAMP-responsive element that binds ATF2/c-Jun. In human endothelial cells, TNF rapidly induces N-terminal domain phosphorylation of both c-Jun and ATF2. Transient overexpression of N-terminal truncated c-Jun or catalytically inactive Jun N-terminal kinase (JNK) 1 and 2 inhibits TNF-induced transcription of an E-selectin but not a kappa B promoter-reporter gene. Transient overexpression of the TRAF2 adaptor protein can activate NF-kappaB and endogenous JNK, whereas N-terminal truncated TRAF2 protein blocks TNF-induced NF-kappa B and JNK activation as well as E-selectin promoter-reporter gene transcription. Transient overexpression of RAC1 or CDC42, but not RAS, constitutively activates JNK and augments TNF-induced E-selectin transcription. Finally, transient overexpression of catalytically inactive JNK or truncated **TRAF2** partially **inhibits** endogenous E-selectin protein expression in human endothelial cells. These data suggest that TNF activates parallel TRAF-NF-kappa B and TRAF-RAC/CDC42-JNK-c-Jun/ATF2 pathways to initiate E-selectin transcription.

L36 ANSWER 15 OF 23 MEDLINE on STN
ACCESSION NUMBER: 97368221 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9221764
TITLE: Assembly and regulation of the CD40 receptor complex in human B cells.
AUTHOR: Kuhne M R; Robbins M; Hambor J E; Mackey M F; Kosaka Y; Nishimura T; Gigley J P; Noelle R J; Calderhead D M
CORPORATE SOURCE: Department of Microbiology, Dartmouth Medical School, Lebanon, New Hampshire 03756, USA.
SOURCE: Journal of experimental medicine, **(1997 Jul 21)** 186 (2) 337-42.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970825
Last Updated on STN: 19970825
Entered Medline: 19970814

AB CD40 is a member of the tumor necrosis factor (TNF) receptor superfamily. Studies with human B cells show that the binding of CD154 (gp39, CD40L) to CD40 recruits TNF receptor- associated factor 2 (TRAF2) and TRAF3 to the receptor complex, induces the downregulation of the nonreceptor-associated TRAFs in the cell and induces an increased expression of Fas on the cell surface. Combined signaling through the interluekin 4 receptor and CD40 induces an increased expression of Fas with a commensurate increase in the level of TRAF2, but not TRAF3, that is recruited to the receptor complex. In contrast, engagement of the membrane immunoglobulin and CD40 limits Fas upregulation and **reduces** the recruitment of **TRAF2**, relative to TRAF3, to the CD40 receptor complex. These studies show that the TRAF composition of the CD40 receptor complex can be altered by signals that influence B cell differentiation.

L36 ANSWER 16 OF 23 MEDLINE on STN
ACCESSION NUMBER: 97258620 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9104814
TITLE: TRAF-interacting protein (TRIP): a novel component of the tumor necrosis factor receptor (TNFR)- and CD30-TRAF signaling complexes that **inhibits TRAF2** -mediated NF-kappaB activation.
AUTHOR: Lee S Y; Lee S Y; Choi Y
CORPORATE SOURCE: The Rockefeller University, New York 10021, USA.
SOURCE: Journal of experimental medicine, **(1997 Apr 7)** 185 (7) 1275-85.

Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ010317; GENBANK-U77844; GENBANK-U77845
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 20000303
Entered Medline: 19970514

AB Through their interaction with the TNF receptor-associated factor (TRAF) family, members of the tumor necrosis factor receptor (TNFR) superfamily elicit a wide range of biological effects including differentiation, proliferation, activation, or cell death. We have identified and characterized a novel component of the receptor-TRAF signaling complex, designated TRIP (TRAF-interacting protein), which contains a RING finger motif and an extended coiled-coil domain. TRIP associates with the TNFR2 or CD30 signaling complex through its interaction with TRAF proteins. When associated, TRIP **inhibits** the **TRAF2**-mediated NF-kappaB activation that is required for cell activation and also for protection against apoptosis. Thus, TRIP acts as a receptor-proximal regulator that may influence signals responsible for cell activation/proliferation and cell death induced by members of the TNFR superfamily.

L36 ANSWER 17 OF 23 MEDLINE on STN
ACCESSION NUMBER: 97188478 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9037063
TITLE: CD30 induction of human immunodeficiency virus gene transcription is mediated by TRAF2.
AUTHOR: Tsitsikov E N; Wright D A; Geha R S
CORPORATE SOURCE: Division of Immunology, Children's Hospital, Department of Pediatrics Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: AI-31541 (NIAID)
AR-43985 (NIAMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1997 Feb 18)** 94 (4) 1390-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 19970407
Entered Medline: 19970327

AB CD30 is a member of the tumor necrosis factor receptor (TNFR) superfamily expressed on activated T and B lymphocytes and natural killer cells. Ligation of CD30 was previously shown to induce NF-kappaB activation and HIV expression in chronically infected T lymphocytes. In this study, we report that two members of the TNFR-associated factor (TRAF) family of proteins, TRAF1 and TRAF2, independently bind to the intracellular domain of CD30 (CD30IC). Transient overexpression of TRAF2, but not TRAF1, induced NF-kappaB activation and HIV-1-long terminal repeat-driven transcription in the T cell line, KT3. Moreover, dominant negative mutants consisting of the TRAF domain of TRAF1 and **TRAF2** **inhibited** CD30 induction of NF-kappaB activation and HIV-1 transcription. These results suggest that CD30 ligation may enhance the expression of HIV via TRAF-2-mediated activation of NF-kappaB.

L36 ANSWER 18 OF 23 MEDLINE on STN
ACCESSION NUMBER: 97008137 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8855313

TITLE: Tumor necrosis factor receptor associated factor 2 is a mediator of NF-kappa B activation by latent infection membrane protein 1, the Epstein-Barr virus transforming protein.
AUTHOR: Kaye K M; Devergne O; Harada J N; Izumi K M; Yalamanchili R; Kieff E; Mosialos G
CORPORATE SOURCE: Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.
CONTRACT NUMBER: 1K11CA01568-04 (NCI)
CA47006 (NCI)
CA67380-02 (NCI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1996 Oct 1)** 93 (20) 11085-90.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U63830
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961125

AB Latent infection membrane protein 1 (LMP1), the Epstein-Barr virus transforming protein, associates with tumor necrosis factor receptor (TNFR) associated factor 1 (TRAF1) and TRAF3. Since TRAF2 has been implicated in TNFR-mediated NF-kappa B activation, we have evaluated the role of TRAF2 in LMP1-mediated NF-kappa B activation. TRAF2 binds in vitro to the LMP1 carboxyl-terminal cytoplasmic domain (CT), coprecipitates with LMP1 in B lymphoblasts, and relocalizes to LMP1 plasma membrane patches. A dominant negative TRAF2 deletion mutant that lacks amino acids 6-86 (TRAF/ delta 6-86) inhibits NF-kappa B activation from the LMP1 CT and competes with TRAF2 for LMP1 binding. **TRAF2** delta 6-86 **inhibits** NF-kappa B activation mediated by the first 45 amino acids of the LMP1 CT by more than 75% but inhibits NF-kappa B activation through the last 55 amino acids of the CT by less than 40%. A TRAF interacting protein, TANK, inhibits NF-kappa B activation by more than 70% from both LMP1 CT domains. These data implicate TRAF2 aggregation in NF-kappa B activation by the first 45 amino acids of the LMP1 CT and suggest that a different TRAF-related pathway may be involved in NF-kappa B activation by the last 55 amino acids of the LMP1 CT.

L36 ANSWER 19 OF 23 MEDLINE on STN
ACCESSION NUMBER: 96323205 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8710854
TITLE: I-TRAF is a novel TRAF-interacting protein that regulates TRAF-mediated signal transduction.
AUTHOR: Rothe M; Xiong J; Shu H B; Williamson K; Goddard A; Goeddel D V
CORPORATE SOURCE: Tularik, Inc., South San Francisco, CA 94080, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1996 Aug 6)** 93 (16) 8241-6.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U59863; GENBANK-U59864
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 20000303
Entered Medline: 19960912

AB Tumor necrosis factor (TNF) receptor-associated factor (TRAF) proteins associate with and transduce signals from TNF receptor 2, CD40, and presumably other members of the TNF receptor superfamily. TRAF2 is required for CD40- and TNF-mediated activation of the transcription factor NF-kappa B. Here we describe the isolation and characterization of a novel TRAF-interacting protein, I-TRAF, that binds to the conserved TRAF-C domain of the three known TRAFs. Overexpression of I-TRAF **inhibits TRAF2**-mediated NF-kappa B activation signaled by CD40 and both TNF receptors. Thus, I-TRAF appears as a natural regulator of TRAF function that may act by maintaining TRAFs in a latent state.

L36 ANSWER 20 OF 23 MEDLINE on STN
ACCESSION NUMBER: 96270609 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8692885
TITLE: The tumor necrosis factor-inducible zinc finger protein A20 interacts with TRAF1/**TRAF2** and **inhibits** NF-kappaB activation.
AUTHOR: Song H Y; Rothe M; Goeddel D V
CORPORATE SOURCE: Tularik, Inc., South San Francisco, CA 94080, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1996 Jun 25)** 93 (13) 6721-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960823

AB TRAF1 and TRAF2 form an oligomeric complex that associates with the cytoplasmic domains of various members of the tumor necrosis factor (TNF) receptor superfamily. TRAF2 action is required for activation of the transcription factor NF-kappaB triggered by TNF and the CD40 ligand. Here we show that TRAF1 and TRAF2 interact with A20, a zinc finger protein, whose expression is induced by agents that activate NF-kappaB. Mutational analysis revealed that the N-terminal half of A20 interacts with the conserved C-terminal TRAF domain of TRAF1 and TRAF2. In cotransfection experiments, A20 blocked TRAF2-mediated NF-kappaB activation. A20 also inhibited TNF and IL-1-induced NF-kappaB activation, suggesting that it may inhibit NF-kappaB activation signaled by diverse stimuli. The ability of A20 to block NF-kappaB activation was mapped to its C-terminal zinc finger domain. Thus, A20 is composed of two functionally distinct domains, an N-terminal TRAF binding domain that recruits A20 to the TRAF2-TRAF1 complex and a C-terminal domain that mediates inhibition of NF-kappaB activation. Our findings suggest a possible molecular mechanism that could explain A20's ability to negatively regulate its own TNF-inducible expression.

L36 ANSWER 21 OF 23 EMBASE on STN
ACCESSION NUMBER: 1998008327 EMBASE
TITLE: TRANCE (Tumor necrosis factor [TNF]-related Activation-induced Cytokine), a new TNF family member predominantly expressed in t cells, is a dendritic cell-specific survival factor.
AUTHOR: Wong B.R.; Josien R.; Soo Young Lee; Sauter B.; Li H.-L.; Steinman R.M.; Choi Y.
CORPORATE SOURCE: Dr. Y. Choi, Rockefeller University, Box 295, 1230 York Ave., New York, NY 10021, United States.
choi@rockvax.rockefeller.edu
SOURCE: Journal of Experimental Medicine, (1997) 186/12

(2075-2080).
Refs: 32
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB TRANCE (tumor necrosis factor [TNF]-related activation-induced cytokine) is a new member of the TNF family that is induced upon T cell receptor engagement and activates c-Jun N-terminal kinase (JNK) after interaction with its putative receptor (TRANCE-R). In addition, TRANCE expression is restricted to lymphoid organs and T cells. Here, we show that high levels of TRANCE-R are detected on mature dendritic cells (DCs) but not on freshly isolated B cells, T cells, or macrophages. Signaling by TRANCE-R appears to be dependent on TNF receptor-associated factor 2 (TRAF2), since JNK induction is impaired in cells from transgenic mice overexpressing a dominant negative **TRAF2** protein. TRANCE **inhibits** apoptosis of mouse bone marrow-derived DCs and human monocyte-derived DCs in vitro. The resulting increase in DC survival is accompanied by a proportional increase in DC-mediated T cell proliferation in a mixed leukocyte reaction. TRANCE upregulates Bcl-X(L) expression, suggesting a potential mechanism for enhanced DC survival. TRANCE does not induce the proliferation of or increase the survival oft or B cells. Therefore, TRANCE is a new DC-restricted survival factor that mediates T cell-DC communication and may provide a tool to selectively enhance DC activity.

L36 ANSWER 22 OF 23 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 128:138041 CA
TITLE: Tumor necrosis factor receptor-associated factor type 2 kinase from human cDNA and its domain structure
INVENTOR(S): Song, Ho Yeong; Rothe, Mike
PATENT ASSIGNEE(S): Tularik, Inc., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9801541	A1	19980115	WO 1997-US11981		19970708	<--
W: AU, CA, JP						
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
US 5874230	A	19990223	US 1996-677862		19960710	
AU 9736564	A1	19980202	AU 1997-36564		19970708	<--
US 5981250	A	19991109	US 1999-252571		19990218	
US 6107074	A	20000822	US 1999-434065		19991105	
PRIORITY APPLN. INFO.:			US 1996-677862	A	19960710	
			WO 1997-US11981	W	19970708	
			US 1999-252571	A1	19990218	

AB The invention provides methods and compns. relating to a novel human tumor necrosis factor receptor-associated factor 2 (TRAF2) kinase protein. The invention provides hybridization probes and primers capable of hybridizing with the disclosed gene, nucleic acid encoding the kinase, methods of making the kinase proteins, and methods of using the compns. in diagnosis and drug screening. Thus, a human kinase protein was initially identified in immunoppts. of TRAF2. Copptg. proteins were purified and subjected ro peptide sequencing to design oligonucleotide probe and primers to isolate human cDNA clones. Identification was confirmed by overexpressing a full-length myc-tagged kinase-encoding cDNA in human 293 cells cotransfected with FLAG-tagged TRAF2 and immunopptg. the lysates with

anti-FLAG and then western blot anal. with anti-myc. A yeast 2-hybrid system was also used to confirm TRAF2 binding and for deletion mutagenesis of kinase. Kinase residues 1-763, residues 1-598, and residues 159-763 are each sufficient to mediate TRAF2 binding, whereas residues 1-567 is not. Human kinase peptides from the 567-598 region are able to **inhibit** kinase-**TRAF2** binding. Sequence anal. further define a kinase domain of residues 159-479. Recombinant kinase was prepared by over-expressing glutathione S-transferase fusion proteins in Escherichia coli and baculovirus expression systems.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 23 OF 23 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 127:342254 CA

TITLE: Protein ligands for the tumor necrosis factor receptor-associated factor (TRAF) and their use in the control of NF-κB activity

INVENTOR(S): Wallach, David; Malinin, Nikolai; Boldin, Mark; Kovalenko, Andrei; Mett, Igor

PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel; Wallach, David; Malinin, Nikolai; Boldin, Mark; Kovalenko, Andrei; Mett, Igor

SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737016	A1	19971009	WO 1997-IL117	19970401 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2250085	AA	19971009	CA 1997-2250085	19970401 <--
AU 9721755	A1	19971022	AU 1997-21755	19970401 <--
AU 732793	B2	20010503		
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1221449	A	19990630	CN 1997-195193	19970401
BR 9708518	A	19990803	BR 1997-8518	19970401
NZ 331902	A	20000228	NZ 1997-331902	19970401
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NO 9804551	A	19981124	NO 1998-4551	19980929 <--
KR 2000005204	A	20000125	KR 1998-707880	19981002
AU 767967	B2	20031127	AU 2001-35080	20010410
AU 767924	B2	20031127	AU 2001-35081	20010410

PRIORITY APPLN. INFO.:		
IL 1996-117800	A	19960402
IL 1996-119133	A	19960826
AU 1997-21755	A3	19970401
WO 1997-IL117	W	19970401

AB Protein ligands for tumor necrosis factor receptor-associated factors (TRAFs) that play a role in the modulation of NF-κB activity and genes encoding them are described. These protein modulate activation of NF-κB by **TRAF2** and TRAF6 and **inhibition** of NF-κB by TRAF3 and also play wider roles by indirectly modulating the activity of other proteins that interact with TRAF. The proteins may

be useful as targets for therapy of diseases associated with NF-κB activity, either by identification of suitable agonists or antagonists or through gene therapy. One of the proteins is NIK a protein kinase that induces NF-κB. CDNAs for TRAF ligands were identified using a yeast two-hybrid system.

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	133.56	133.77

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.32	-1.32

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